REMARKS

Claims 1-8, 16, 28, and 29 are pending and under consideration. No amendments are proposed herein.

Regarding 35 U.S.C. § 102

Applicants respectfully traverse the rejection of claims 1-8, 16 and 28-29 under 35 U.S.C. rejected under 35 U.S.C. 102(a) as being anticipated by Sen et al., *Arthritis & Rheumatism* 44: 772-781 (2001).

The principle of "inherency," in the law of anticipation, requires that any information missing from the reference would nonetheless be known to be present in the subject matter of the reference, when viewed by persons experienced in the field of the invention. However, "anticipation by inherent disclosure is appropriate only when the reference discloses prior art that must *necessarily* include the unstated limitation, [or the reference] cannot inherently anticipate the claims." *Transclean Corp. v. Bridgewood Servs., Inc.*, 290 F.3d 1364, 1373 (Fed. Cir. 2002) (emphasis in original); *Hitzeman v. Rutter*, 243 F.3d 1345, 1355 (Fed. Cir. 2001) ("consistent with the law of anticipation, an inherent property must necessarily be present in the invention described by the count, and it must be so recognized by persons of ordinary skill in the art"); *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999) (that a feature in the prior art reference "could" operate as claimed does not establish inherency).

Thus when a claim limitation is not explicitly set forth in a reference, evidence "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." *Continental Can Co.*, 948 F.2d at 1268. It is not sufficient if a material element or limitation is "merely probably or possibly present" in the prior art. *Trintec Indus., Inc. v. Top-U.S.A. Corp.*, 295 F.3d 1292, 1295 (Fed. Cir. 2002). *See W.L. Gore v. Garlock, Inc.*, 721 F.2d at 1554 (Fed. Cir. 1983) (anticipation "cannot be predicated on mere conjecture respecting the characteristics of products that might result from the practice of processes disclosed in references"); *In re Oelrich*, 666 F.2d 578, 581 (CCPA 1982) (to anticipate, the asserted inherent function must be present in the prior art).

The claims require that the recited antibody specifically binds to *at least one* epitope in an amino terminal extracellular domain of the frizzled 5 receptor expressed *on a malignant cell*,

wherein the amino terminal extracellular domain is SEQ ID NO:68 and that the antibody *inhibits growth of the malignant cell that expresses the frizzled 5 receptor.*

Set forth below is the amino acid sequence of human frizzled-5, which is 585 amino acids in length. The bolded portion of 235 amino acids corresponds to the amino terminal extracellular domain designated SEQ ID NO: 68. The red type face amino acids, a 20 amino acid segment spanning residues 197 to 218, correspond to the peptide used by Sen et al. to prepare the polyclonal antibodies used in the cited reference. There is no basis to assert that the polyclonal antibodies described by Sen et al., which were raised using a very small portion of SEQ ID NO:68, inhibit the growth of a malignant cell. Since only a 20 amino acid peptide was injected into rabbits, any epitope recognized by the polyclonal antibodies must fall within this limited region and it is not clear that these antibodies have the characteristic of growth inhibition of a malignant cell . Accordingly, since it is not sufficient if the recited elements/characteristics are "merely probably or possibly present" in the prior art, this rejection should be withdrawn.

001 **marpdpsapp sllllllaql vgraaaaska pvcqeitvpm crgigynlth mpnqfnhdtq**
061 **deaglevhqf wplveiqcsp dlrfflctmy tpiclpdyhk plppcrsvce rakagcsplm**
121 **rqygfawper mscdrlpvlg rdaevlcmdy nrseattapp rpfpakptlp gppgapasgg**
181 **ecpaggpfvc kcrepfvpil keshplynkv rtgqvpncav pcyqpsfsad ertfatfwig**
241 lwsvlcfist sttvatflid mdtfryperp iiflsacylc vslgflvrlv vghasvacsr
301 ehnhihyett gpalctivfl lvyffgmass iwwvilsltw flaaamkwgn eaiagygqyf
361 hlaawlipsv ksitalalss vdgdpvagic yvgnqnlnsl rrfvlgplvl yllvgtlfll
421 agfvslfrir svikqggtkt dkleklmiri giftllytvp asivvacyly eqhyreswea
481 altcacpghd tgqprakpey wvlmlkyfmc lvvgitsgvw iwsgktvesw rrftsrcccr
541 prrghksgga maagdypeas aaltgrtgpp gpaatyhkqv slshv

Regarding 35 U.S.C. § 103

Applicants respectfully traverse the rejection of claims 1-8, 16 and 28-29 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Tanaka et al., *Proc. Natl. Acad. Sci. USA* 95:10164-10169 (1998) in view of U.S. Patent No. 5,677,171 (Hudziak et al.).

A prior art reference that "teaches away" from the claimed invention is a significant factor to be considered in determining obviousness; however, "the nature of the teaching is highly relevant and must be weighed in substance." *In re Gurley*, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994) Applicants argued that Tanaka et al. show that the frizzled 5 receptor *lacks* the differential expression in human esophageal carcinomas that was observed

with FzdE3 and was the very reason for the authors of Tanaka et al. to conclude a potential role for FzdE3. Applicants maintain that this provides a strong teaching away. The Examiner has again deemed Applicants response unpersuasive without addressing Applicants' arguments and simply repeats the assertions of the previous Office Action. Instead of a substantive rebuttal, the Examiner again compares the teaching of Applicants specification to Tanaka et al. arguing, *inter alia*:

> The disclosure of Tanaka et al. is similar in that the instant specification discloses frizzled 2 data (Fig. 5 and 6), while Tanaka et al., discloses frizzled 3 data.

Applicants respectfully reiterates that the Examiner is impermissibly comparing the Tanaka et al. reference to the Applicants' disclosure. It is Applicants' claims that are rejected and that have to be compared to any cited references. Whether or not the specification includes frizzled 2 data is irrelevant to the question of whether or not Tanaka et al., in combination with Hudziak et al., which effectively describes conditions for producing antibodies that are based on known tumor enhancing growth factor activities of the targets that do not include the frizzled 5 receptor, render obvious the claimed invention.[1]

In sum, Applicants maintain that Tanaka et al. teaches way from the claimed invention by showing that the frizzled 5 receptor lacks the differential expression in human esophageal carcinomas that was observed with FzdE3 and by proposing a potential role for FzdE3 in the pathogenesis of the condition without making a similar prediction with regard to frizzled 5. The silence of Tanaka et al. on frizzled 5 is compounded by the author's admission that the role of frizzled 5 in cancer was unexplored (see citation above). Therefore, Tanaka et al. effectively discourages targeting the frizzled 5 receptor and represents a teaching away from the claimed invention.

In view of the above, Applicants respectfully request removal of claims 1-8, 16 and 28-29 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Tanaka et al., *Proc. Natl. Acad. Sci. USA* 95:10164-10169 (1998) in view of U.S. Patent No. 5,677,171.

CONCLUSION

In light of the remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned attorney if there are any questions or if it is believed that a telephonic interview may expedite prosecution.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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[1] It is likewise irrelevant to the question of patentability under section 103 of the code whether or not SEQ ID NO:68 is described in the art. See Office Action mailed 2/25/08 at p.4 and again Office Action mailed November 13, 2008, at p.3. Applicants are not claiming SEQ ID NO:68 as a novel composition.